IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

PAR PHARMACEUTICAL, INC., PAR STERILE PRODUCTS, LLC, and ENDO PAR INNOVATION COMPANY, LLC Plaintiffs, v. SANDOZ INC. Defendant.	Case No. 3:18-cv-14895-BRM-DEA

PLAINTIFFS' SUPPLEMENTAL CLAIM CONSTRUCTION BRIEF

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Pursuant to the Court's instructions following the *Markman* hearing conducted on January 21, 2020, Par submits this supplemental brief setting forth its closing arguments concerning the proper construction of the four remaining disputed claim terms.

I. THE "ADMINISTERING" TERMS

Injectable dosage forms can be "administered" to patients in a variety of ways, including subcutaneously, intra-muscularly, and intravenously in either diluted form or undiluted form. In the related Delaware proceedings, Judge Connolly correctly construed the "administering" terms in accordance with their ordinary meaning as encompassing all forms of administration—including intravenous administration in which the claimed vasopressin dosage form is diluted in a diluent (IV bag) before being injected into the patient. *See* Ex. 7. Indeed, that form of "administering" is the "Illustrative Regimen" taught in the patents (*see, e.g.*, '526 patent (Ex. 3) at 59:50-60:37) and the one known by persons of skill in the art (POSAs) to be the most common method, by far, for "administering" vasopressin in the real world (*see* Coralic Decl. (Ex. 20)). Judge Connolly rejected the very same arguments that Sandoz now makes for excluding that form of "administering" from the disputed claims, and this Court should do the same.

Sandoz argues that its construction is dictated by the claims. Not so—indeed, the opposite is true. Sandoz points to the '239 patent claims, which include an express dilution step and argues that the claims in the other patents "say nothing about dilution" and make "no mention of dilution or IV drip." Sandoz Reply at 2, 3. Sandoz further argues that "[t]he '239 patent expressly recites administering a 'diluted unit dosage form' while the '478, '209, '526 and '223 patents are silent on dilution." *Id.* at 5. Sandoz is wrong. In fact, there is extensive discussion of dilution in those patents, and dependent claims in those patents do expressly include dilution steps similar to those in the '239 patent claims. *See, e.g.*, Ex. A (Par Markman PPT) at 19-25; '526 patent (Ex. 3) claims 16-19; '223 patent (Ex. 6) claims 11, 18.

At the hearing, Sandoz focused on the fact that the concentration of the claimed vasopressin dosage forms after dilution (*i.e.*, from "about 0.21 µg/mL to about 2.1 µg/mL") is below the concentration of vasopressin recited in the disputed independent claims (from "about 0.01 mg/ML to about 0.07"), arguing that those independent claims therefore cannot encompass administration of the claimed vasopressin compositions in diluted form. Again, however, the claims themselves belie Sandoz's argument. In particular, dependent claims 16 and 17 of the '526 patent, which depend from independent claim 1 thereof, recite the following:

> **16**. The method of claim **1**, wherein the pharmaceutical composition is diluted in a diluent prior to administration to the subject.
>
> **17**. The method of claim **16**, wherein the pharmaceutical composition is diluted to a concentration of from about 0.21 µg/mL to about 2.1 µg/mL of vasopressin or the pharmaceutically acceptable salt thereof.

Thus, analysis of the claims directly contradicts Sandoz's arguments and confirms the correctness of Judge Connolly's ruling. The fact that the '239 patent claims specifically recite administration in diluted form only means that those particular claims are expressly limited to that form of administration. By contrast, the independent claims in other patents that contain no such restriction are not limited in that fashion and broadly encompass all modes of administration. In that respect, these claims are like those at issue in *Arlington Industries, Inc. v. Bridgeport Fittings, Inc.*, 632 F.3d 1246 (Fed. Cir. 2011), where an independent claim in one patent recited a "split circular spring metal adaptor," while the claim in another patent "omit[ted] the 'split' modifier." *Id.* at 1254. The Federal Circuit held that "[t]hus, unlike the adaptor of claim 12 of the '164 patent, the spring metal adaptor of claim 8 can either be split or unsplit." *Id.* As the Federal Circuit explained in *Chrimar Holding Company, LLC v. ALE USA Inc.*, 732 F. App'x. 876 (Fed. Cir. 2018), "[i]t is hardly unknown for one set of claims to use language that picks out one among several embodiments, especially where other claims (perhaps in the same or

related patents) claim more broadly or focus on other embodiments." *Id.* at 884. That is the situation we have here—unlike the "administering" step of '239 claim 1, which expressly restricts the claim to administration of the claimed dosage form in diluted form, the "administering" limitations of the independent claims in the remaining patents encompass administration in either diluted or undiluted form.

This is further confirmed by the dependent claims cited above, which depend from the independent claims and expressly recite administration via diluting the dosage form in a diluent. Thus, as Judge Connolly held, the doctrine of claim differentiation compels the conclusion that the disputed "administering" claims do not exclude administration of the claimed compositions in diluted form. *See, e.g., Wright Med. Tech., Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1445 (Fed. Cir. 1997) ("[W]e must not interpret an independent claim in a way that is inconsistent with a claim which depends from it."). *See also* Par Op. Br. at 14-16; Par Reply at 7-8.

Sandoz's other principal argument at the *Markman* hearing was to point to embodiments which make no mention of dilution, and contrast them with others that do, as if the two are mutually exclusive. *See, e.g.,* Sandoz Markman Slide 18. That argument, however, puts the cart before the horse—it assumes that the embodiments that do not expressly mention dilution somehow exclude dilution, rather than encompassing all forms of "administering" the claimed vasopressin compositions, including intravenous administration via either an IV drip or an IV push (and also intramuscular and subcutaneous administration as well, among others). Eagle made the same argument in Delaware, citing the same evidence, and Judge Connolly properly rejected it. *See* Par Reply at 7-10. The intrinsic evidence shows that consistent with the illustrative treatment regimen taught in the specification, the patentees intended that the disputed "administering" steps would include, rather than exclude, continuous intravenous administration of the recited vasopressin compositions via an IV drip. No example in the patents specifically

describes administering any vasopressin composition in concentrated form, without dilution, and construing the disputed claims as excluding dilution would improperly exclude the preferred embodiment taught in the patents. *See, e.g.,* Par Op. Br. at 11-12, 16-17.

II. "VASOPRESSIN"

"When the patentee acts as its own lexicographer, that definition governs." *Continental Circuits LLC v. Intel Corp.*, 915 F.3d 788, 796 (Fed. Cir. 2019) (citing *Phillips v. AWH Corp.*, 415 F.3d 1303, 1316 (Fed. Cir. 2005) (en banc)). Here, the patents include a four-page "Sequence Listing" that sets forth the chemical formula and structure for the various peptides described in the patents, including that of the claimed vasopressin and its related impurities. *See, e.g.*, '478 patent (Ex. 1) at cols. 25-32. Indeed, the PTO regulation cited by Sandoz at the hearing specifically provides that "[p]atent applications which contain disclosures of nucleotide and/or amino acid sequences [such as, *e.g.*, for peptides like vasopressin] ***must contain*** . . . a paper or compact disc copy . . . disclosing the nucleotide and/or amino acid sequences and associated information using the symbols and format in accordance with the requirements of §§ 1.822 and 1.823," referred to as the "Sequence Listing." 37 CFR § 1.821(c) (emphasis added). The patentees did just that, and throughout the patents, they repeatedly defined the vasopressin of their inventions by reference to its listing as "SEQ ID NO. 1":[1]

> Vasopressin is a nonapeptide, illustrated below (SEQ ID NO. 1):

* * * * *

[1] A patentee's lexicography need not be in "explicit definitional format," but instead may be "by implication" based on the patentee's "consistent use in the specification." *Irdeto Access, Inc. v. Echostar Satellite Corp.*, 383 F.3d 1295, 1300-1302 (Fed. Cir. 2004); *Bell Atl. Network Servs., Inc. v. Covad Commc'ns Grp., Inc.*, 262 F.3d 1258, 1268 (Fed. Cir. 2001). That is what we have here.

Vasopressin and associated degradation products or peptides are listed in TABLE 1 below. All amino acids are L-stereoisomers unless otherwise denoted.

TABLE 1

Name	Sequence	SEQ ID NO.
Vasopressin (AVP; arginine vasopressin)	CYFQNCPRG-NH_2	1

* * * * *

TABLE 3 below details the chemical formula, relative retention time (RRT in minutes), molar mass, and structure of vasopres sin and detected impurities.

TABLE 3

Name	Formula	Appr. RRT	Molar Mass (g)
Vasopressin (Arginine Vasopressin, AVP) CYFQNCPRG-NH_2 SEQ ID NO.: 1 (disulfide bridge between cys residues)	$C_{46}H_{65}N_{15}O_{12}S_2$	1.00	1084.23

* * * * *

The chemical name of vasopressin is Cyclo (1-6) L-Cysteinyl-L-Tyrosyl-L-Phenylalanyl-L-Glutaminyl-L-Asparaginyl-L-Cysteinyl-L-Prolyl-L-Arginyl-L-Glycinamide. Vasopressin is a white to off-white amorphous powder, freely soluble in water. The structural formula of vasopressin is:

SEQ ID NO.: 1

H—Cys-Tyr-Phe-Glu(NH_2)-Asp(NH_2)-Cys-Pro-Arg-Gly-NH_2
1 2 3 4 5 6 7 8 9

See, e.g., Ex. A (Par Markman PPT) at 35-37; '478 patent (Ex. 1) at 1:45-65, 3:36-45, 18:40-52, 23:27-38.[2]

[2] In doing so, the patentees were complying with the requirement of the PTO regulations that "[w]here the description or claims of a patent application discuss a sequence that is set forth in the 'Sequence Listing' in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by 'SEQ ID NO:' in the text of the description or claims." 37 CFR § 1.821(d). The evident purpose of the PTO regulation is to ensure clarity as to the chemical formula and structure of any amino acid sequences taught and claimed in the patents, and that is why the patentees defined the vasopressin of their invention by

Sandoz's arguments for rejecting the patentees' express definition of vasopressin by reference to SEQ ID NO. 1 are unavailing.

Sandoz's first argument is that Sequence Listing is non-limiting because the paragraph in the specification that appears just before the Sequence Listing refers to "[t]he following non-limiting embodiments provide illustrative examples of the invention," as if that paragraph is referring to the "Sequence Listing" at the end of the specification. *See* Sandoz Markman Slides 51-52. That is false. As required by the PTO regulation which Sandoz itself cited, the Sequence Listing is to be provided by the patentee "as a separate part of the disclosure" (37 CFR § 1.821(c)) that must "also be submitted in computer readable form" (37 CFR § 1.821(e)). In other words, it is a separate and distinct, standalone section of the specification submitted separately to the PTO. That is what the patentees did here—*see, e.g.*, Ex. A hereto (PTO confirmation of electronic filing of separate Sequence Listing for '478 patent); Ex. B hereto (excerpt of '478 patent application, showing the paragraph cited by Sandoz followed by the then-pending claims, not the Sequence Listing). That is why there is a solid dark line that spans the width of the page between the description of the "non-limiting embodiments" cited by Sandoz (which refers to the embodiments in the paragraph that follows) and the Sequence Listing. *See* Sandoz Markman Slide 51, citing the '239 patent (Ex. 2) at cols. 25-26.

Sandoz also cites to the description in the specification of the fact that vasopressin naturally occurs in humans. *See* '478 patent (Ex. 1) at 2:22-25. However, the cited statement merely provides background information, and does nothing to change the fact that when the patentees were talking about the vasopressin of their claimed formulations, they referred to it by

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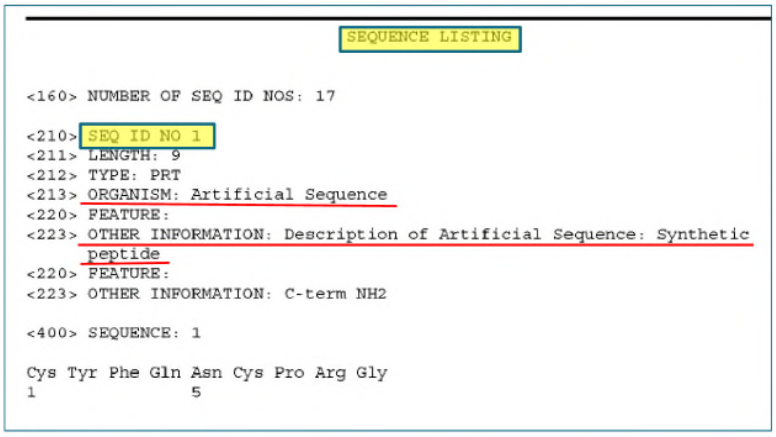
specific reference to SEQ ID NO. 1. Moreover, contrary to Sandoz's assertion at the hearing, the reference to the SEQ ID NO. need not be included in the claims themselves—the regulation provides that "reference must be made to the sequence by use of the sequence identifier, preceded by 'SEQ ID NO:' *in the text of the description* or *claims*." *Id.* (emphasis added).

reference to its SEQ ID NO.—as required by the above-cited PTO regulations.

Finally, for the reasons discussed during the hearing, and as shown in Par's Markman Slides (at 38-46), the claimed vasopressin of SEQ ID NO. 1 is synthetic, arginine vasopressin. Indeed, Sandoz's counsel confirmed at the hearing that the "Arg" referred to in the chemical diagrams and sequence listings cited by Par make clear that the patentees were referring to *arginine* vasopressin, and Sandoz had no comeback for the fact that SEQ ID NO. 1 expressly states that the cited vasopressin is a "Synthetic peptide":



SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 17

<210> SEQ ID NO 1
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<223> OTHER INFORMATION: Description of Artificial Sequence: Synthetic peptide
<220> FEATURE:
<223> OTHER INFORMATION: C-term NH2

<400> SEQUENCE: 1

Cys Tyr Phe Gln Asn Cys Pro Arg Gly
1 5

Ex. A (Par Markman PPT) at 43; '478 patent (Ex. 1) at col. 25-26.

III. "CONSISTS ESSENTIALLY OF"

Sandoz's counsel conceded at the hearing that with respect to this term, it is Sandoz's burden to prove by clear and convincing evidence that the disputed claim, viewed in light of the specification and prosecution history, fails to "inform those skilled in the art about the scope of the invention with reasonable certainty." *See Nautilus, Inc. v. Biosig Instruments, Inc.*, 572 U.S. 898, 910 (2014); *Microsoft Corp. v. i4i Ltd. P'ship*, 564 U.S. 91, 102 (2011).

Yet, Sandoz relies entirely on lawyer argument, ***without citing any expert evidence***. In effect, Sandoz seeks summary judgment of invalidity regarding technical issues relating to what would be known and understood by a POSA, without the benefit of any expert testimony or

discovery. Sandoz's lawyer argument is insufficient to meet its heavy burden and should be rejected by the Court.

When claims use "consists essentially of" transition, as here, two questions arise: (1) what are the basic and novel properties of the claimed inventions? and (2) does a particular unlisted ingredient in the accused product materially affect those basic and novel properties? *See, e.g., HZNP Meds. LLC v. Actavis Labs. UT, Inc.*, 940 F.3d 680, 695 (Fed. Cir. 2019); *PPG Indus. v. Guardian Indus. Corp.*, 156 F.3d 1351, 1357 (Fed. Cir. 1998). The first can be decided as a matter of claim construction (though courts sometimes defer until time of trial), but the second is an infringement question for the factfinder. *Id.*

As to the first question, the intrinsic evidence clearly demonstrates that the basic and novel characteristics are those that Par has identified: stability, pharmaceutical acceptability, effectiveness in treating hypotension, and suitability for intravenous injection. Sandoz's arguments focus on the property of stability.[3] With respect to that property, the specification explains the problems with the prior art as being that vasopressin degrades in aqueous solutions and then-current formulations had "poor long-term stability." '478 patent (Ex. 1) at 1:22-25, 3:1-66. The patents describe extensive work by Par to evaluate the impact of various formulation changes on stability, and all of the figures they cite relate to the stability of vasopressin and the identification and quantification of impurities in vasopressin formulations. *See, e.g., id.* at 15:26-26:5, Figs. 1- 10. The patentees then assert that their inventive formulations "provide advantages in stability, . . .," and that, unlike the prior art, those

[3] It is indisputable that the patents are directed to pharmaceutical products used to treat hypotension that are intended for intravenous administration. Thus, Sandoz cannot seriously challenge that the latter three properties are among basic and novel properties of the invention. Indeed, the specification itself makes clear that additional excipients (*i.e.* ingredients) added to the claimed inventions must be "pharmaceutically-acceptable." '478 patent (Ex. 1) at 15:26-40.

compositions "can be formulated for long-term storage." *Id.* at 5:52-55, 15:26-29. Then, during prosecution, the patentees overcame the examiner's obviousness rejections by demonstrating enhanced stability of the claimed inventions and pointing the examiner to the benefits associated therewith. *See, e.g.*, Ex. 14 at 5-6; Ex. 15 at 6-8; Ex. 16 at 9- 13; Ex. 19 at ¶¶ 29-30. Thus, there can also be no serious dispute that stability was identified by the patentees as a basic and novel characteristic of the claimed invention.[4]

Sandoz asserts that the property of stability is itself indefinite, but cites no expert or other evidence to meet its burden to demonstrate that a POSA would not be able to understand the scope of the claims—*i.e.*, whether the inclusion of an unrecited ingredient "materially affects" the stability of the formulation at issue. Thus, their argument fails as a matter of law. Sandoz cited no case invalidating a patent on such grounds without expert evidence. At the hearing, Sandoz claimed that the Federal Circuit did not rely on expert evidence in *HZNP*. That is false. The Federal Circuit noted that the district court "found persuasive the testimony of Actavis's expert that a POSITA would not know under what standard to evaluate the drying rate." 940 F.3d at 697. Based on that, among other things, the Federal Circuit held that the "district court did not err" in "concluding that the phrase 'consisting essentially of' was indefinite based on its finding that the basic and novel property of 'better drying time' was indefinite ***on this record***." *Id.* at 698-99 (emphasis added). On the record here, there is no factual basis on which the Court could conclude that the property of stability is indefinite in view of the perspective and knowledge of a POSA.[5]

[4] Sandoz argues that the properties cited by Par are not "novel," but that contradicts the prosecution history and raises issues of validity not claim construction that are not ripe or proper for resolution at this stage of the proceedings.

[5] Indeed, the intrinsic evidence demonstrates just the opposite. The teachings, data and testing cited in the specification and declarations submitted during prosecution explain how the

IV. "WHEREIN THE IMPURITIES ARE DETERMINED BASED ON [THE SPECIFIED HPLC METHOD]"

This disputed limitation appears only in two dependent claims, each of which depends from an independent claim that recites a particular property of the claimed vasopressin compositions—*i.e.*, that they have specified impurities in amounts that fall within a particular concentration range. To infringe, the accused product must have that property, meaning that it must have the specified impurities in the specified amounts. The central issue is whether disputed claim limitations recite a requirement that is part of the act of infringement itself (Sandoz's position) or specify the proof required to demonstrate that a particular formulation has the impurities recited in the independent claims (Par's position). It is the latter. This is clear from the structure of the claims. Independent claim 1 of the '785 patent is a composition claim that is infringed when someone makes, uses or sells a vasopressin product that has the recited properties, including the specified impurities. Dependent claim 2 then recites that the presence of those impurities is to be "determined based on" a particular HPLC method. It does not add a method step to the composition claim; it simply recites the type of proof that is to be used to determine whether a formulation at issue has the required properties. Likewise, independent claim 1 of '209 patent recites a method of treating hypotensive patients, and the HPLC test of dependent claim 2 is not part of the method of treating patients; it is how one is to determine whether an accused formulation used to treat patients has the required impurity properties.

V. CONCLUSION

For all the forgoing reasons, the Court should adopt the constructions set forth by Par.

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patentees evaluated the stability of vasopressin formulations and why they concluded that their inventive formulations had improved stability over other, alternative formulations. *See e.g.*, '478 patent at 5:52-60, 15:44-21:3; Ex. 17 (Declaration of Sunil Vandse, Aug. 11, 2015) ¶¶ 3-10; Ex. 18 (Declaration of Sunil Vandse, Jan. 22, 2016) ¶¶ 4-14; Ex. 19 (Declaration of Vinayagam Kannan, Mar. 31, 2016) ¶¶ 4-24.

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